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Glykosid ester and their production as well as use in cosmetics, Pharmaceutical products and Nahrungs- bzw. Feeds

The present invention concerns new, biological active < RTI ID=1.1> Glykosid ester, < /RTI> Method to their production, these junctions contained cosmetic and/or pharmaceutical preparing as well as these bonds contained Nahrungs- und feed.

In the Kosmetik becomes ever more important the application of active substances. With the active substances, which so far already find application in the Kosmetik, it does not concern always natural substances. The optimization of known active substances and the production of new active substances are subject matter of many research work.

In the broadest sense active substances such cloths are occurring, those in relatively small quantities or supply-large physiological effect to unfold can. Here is to hormones, vitamins, enzymes, trace elements etc. to think, in addition, of medicines (drugs), < RTI ID=1.2> Fodder additives, Düngemittel< /RTI> and pesticides. Pretty often one can observe also synergism.

Glykoside and < RTI ID=1.3> arylaliphatische Glykosidester< /RTI> Those inventive accomplished derivatizations obtain an improved effect as well as an increased bioavailability, how it became already early shown at the example of Salicinderivaten.

Many natural occurring Alkyl- und of phenol glucosides show antiviral, antimicrobial and partial antiinflammatorische effects. They are however often bioavailable due to their polarity a little and/or. their selectivity is too small.

For example Salicin (a glycosidic active substance from the pasture crust) is < RTI ID=1.4> nichtsteroidales antiinflammatorisches< /RTI> Agenz (NSAIA), which shows remarkably improved effectiveness after derivatization (esterifications). Recently the synthesis new aryl-aliphatic Salicinester succeeded such as Phenylacetoyl Salicin or Phenylbutyroyl Salicin, whereby the esterification preferred at the primary OH-groups of the Salicins (first at the sugar then at the benzyl remainder) in the Salicin made. Due to the aryl-aliphatic remainder the material transfer is improved to the effect place and the selectivity of the effect increased. Thus these derivatives inhibitieren contrary to unmodified < RTI ID=2.1> Salicin< /RTI> prefered < RTI ID=2.2> Prostaglandinsynthase< /RTI> 2 (smaller danger of side effects) (Ralf T. Petrol, biotechnological production and characterization more again pharmaceutical more active < RTI ID=2.3> Glykolipide, < /RTI> Thesis < RTI ID=2.4> (1999) < /RTI> ISBN 3-86186-258-1).

In addition Ericaceae became, z from excerpts of the plants of the species. B. from the bear grape/cluster (Arctostaphylos uva ursi L.), the Glykosid Arbutin insulated, which strike-lightening effect shows. This Glykosid < a certain; RTI ID=2.5> biotechnologisches< /RTI> Interest is used, there it in Japan because of its lightening effect under the Inhibierung of the Melaninbiosynthese (inhibition of the key enzyme tyrosinase) in considerable quantity (1-2 t per year) in cosmetics. While in the European market the preparations rather approximately < RTI ID=2.6> Old marks, liver flecken< /RTI> and/or.

▲ top

Summer rungs used are < , are in the asiatic market the ideals of beauty of one; RTI ID=2.7> bright makellosen< /RTI> Skin by whole-physical treatment achieved become.

< RTI ID=2.8> Alkylpolyglucoside< /RTI> (APG) Alkylpolyglucoside (APG), become as phosphate-free Neutralenside and. A. Detergents and cosmetics added (on the basis of regenerating raw materials). 1-7 glucose units is glycosidic linked with a Fettalkohol (mostly 12 C-atoms):

EMI 2.1

PUFAs and CLAs natural one of oils (z. B. from sunflower oil, linseed oil, < RTI ID=2.9> Oil tree oil) < /RTI> with an high proportion at polyungesättigten fatty acids (English: polyunsaturated fatty acids, PUFAs) become used in the Kosmetik and Dermatologie. The PUFAs belongs in the diet to the group of the essential fatty acids and shows additionally a positive effect with the tray in the prophylaxis of arteriosclerosis. Besides are also pharmaceutical effects of importance: They can do antiinflammatorische (inhibition Prostaglandin- bzw. Leukotriensynthese), in addition, a thrombolytische and hypotensive effect exhibit.

Inventive one becomes PUFA defined as a multiple insatiated fatty acid with 16 to 26 C-atoms, whereby the fatty acid exhibits at least four insulated and/or at least two conjugated double bonds. Examples for PUFAs are altogether twelve < to the Linolsäure those; RTI ID=3.1> (cis, < /RTI> cis, 9,12-Octadecadiensäure) isomers Octadecadiensäuren (in nature occur), those over conjugated double bonds at the C-atoms 9 and 11.10 and 12, or 11 and 13 order.

This isomers of the Linolsäure (z. B. cis, trans, 9,11-Octadecadiensäure, trans, cis, 10,12-Octade-cadiensäure, cis, cis, 9,11-Octadecadiensäure, trans, cis, 9,11 Octadecadiensäure, trans, trans, 9,11-Octadecadiensäure, cis, cis, 10,12 Octadecadiensäure, cis, trans, 10,12-Octadecadiensäure, trans, trans, 10,12 Octadecadiensäure) can be manufactured on conventional pathways by means of chemical isomerization of the Linolsäure, whereby these reactions lead exclusive

composition most different to CLA mixtures in dependence of the reaction conditions (z. B. Edenor UKD 6010, < RTI ID=3.2> Handle KGaA). < /RTI>

Due to its conjugated double bonds this isomers Octadecadiensäuren becomes also as " conjugated linoleic acids " (CLAs) referred.

One receives it to natural way as mixture major from milk and meat from ruminants (5 mg/g < RTI ID=3.3> Fat), < /RTI> in those it by the Pansenbakterium Butyrivibrio < RTI ID=3.4> fibrisolvens< /RTI> are synthesized.

The effect of the CLAs is very versatile. They show inhibitive effect with the Karzinogenese and with the Artherogenese. They show further an anti-oxidative effect by Furanbildung, which plays an important role with the prevention of crayfish and koronan heart diseases (KHKen). The Vermehrung Muskel-und bone mass through < RTI ID=3.5> Fettdepot reduzierende< /RTI> Characteristics to that to an increased food utilization application in the range leads and finds Nahrungsmittel-und < RTI ID=4.1> Futtermittelindustrie.< /RTI> This effect can on an increased Fatty acid oxidizing in Muskel-und < RTI ID=4.2> Fettzellen< /RTI> recycled become.

A further application of these CLAs than isomeric mixture follows the precursor of the Entzündungsmediators from their competent effect than antiinflammatorische agents, there it due to their structural distorting shank to the arachidonic acid.

Prostaglandin, die zur Biosynthese der Prostaglandine benötigten Desaturasen kompetitiv hemmen können. They displace additionally the precursors Arachidon and Eicosansäure aus den Phospholipiden und hemmen die Umwandlung der Arachidonsäure in die Eicosansäure und damit die Umwandlung in die Prostaglandine.

Although in the literature already numerous pharmakologisch effective cloths are described, those for example in < RTI ID=4.3> Entzündungskaskade< /RTI> engage, exists further a need at better effective active substances poor in side effects.

A need at active substances with a good absorbableness and a quick penetration continues to exist into the skin, which besides good into pharmaceutical or cosmetic formulations be trainable must.

The object, which is the basis for the present invention, consisted thus of it, such side effect-poor, good working and good those which can be processed and too < RTI ID=4.4> applizierenden< /RTI> To make available materials.

< RTI ID=4.5> Glykoside< /RTI> and certain < RTI ID=4.6> Glykosidester< /RTI> are z. B. aus der Natur bekannt. Known (neither from plants, microorganisms or animal cells still synthetic prepared) are not however the here described esters, in particular PUFA and CLA ester, from insatiated fatty acids with sugars or Glykosiden, with those at least one of the hydroxyl groups of the sugar with (insatiated) Carbonbzw. Fatty acid third is.

Überraschenderweise wurde von den Erfindern gefunden, dass bestimmte Ester, insbesondere Ester von ungesättigten Fettsäuren mit Zuckern oder Glykosiden eine gegenüber den bekannten Einzelkomponenten (Fettsäure bzw. < RTI ID=4.7> Sugar/Glykosid) < /RTI> improved biological availability, amplified effect and/or a broadened effect spectrum exhibit. Preferably made < RTI ID=4.8> Esterbildung< /RTI> mittels der primären Hydroxylgruppe des Zuckers/Glykosids ; however also the remaining OH-groups at the sugar or eventual existing OH-groups in < can; RTI ID=5.1> Aglykon< /RTI> (z. B. Hydroxyrest in the case of the Arbutins) for the esterification to be used.

By the provision of the bonds of the present invention the inventors knew solve the problem posed.

The connections of the present invention are esters < RTI ID=5.2> aligemeinen formula (I) < /RTI> : < RTI ID=5.3> ACn O Z o r ", (I), < /RTI> where R a hydrogen, a one < over one; RTI ID=5.4> Etherbrücke< /RTI> at the sugar bound branched or straight-chain < RTI ID=5.5> C8-C2o-Alkyl, < /RTI> one Arylalkyl or a substituted or a unsubstituierten < RTI ID=5.6> C6-Co-Arylrest represents, < /RTI> where Z (sugar) stands for a mono, a disaccharide or a polysaccharide, which are n-multiple ester-like with AC substituted and, if R does not stand for hydrogen, acetalisch to the remainder R bound, where AC a multiple insatiated < RTI ID=5.7> Cr5-C25-Acylrest< /RTI> with at least 4 insulated and/or at least two conjugated double bonds or it represents an aryl-aliphatic remainder with 1-4 groups of groupgroups between group of esters and aromatic ring where m an integral number (1.2.3,?) including 0 it is where n an integral number (1.2.3,?), however 0, is not < , under the condition; RTI ID=5.8> that Z-O-Rm< /RTI> not for Salicin, which is < RTI ID=5.9> 2-Hydroxymethyl-phenyl) - ss-< /RTI> glucopyranosid, steht.

Bevorzugt als Fettsäuren sind CLAs und Stearidonsäure, besonders bevorzugt die Octadecadiensäuren, die über konjugierte Doppelbindungen an den C-Atomen 9 und 11,10 und 12 oder 11 und 13 verfügen, insbesondere die cis, trans, 9,11-und die cis, cis, 9,11-Octadecadiensäure.

EMI5.1

Stearidonsäure (CAS 20290-75-9); 6,9,12,15-Octadecatetraenoic acid, (6Z, 9Z, < RTI ID=5.10> 1 2Z, 1 5Z) - (9Cl) < /RTI>

As sugar mono, Di- und Oligosaccharide, in particular D glucose, come D Galactose, D-xylose, D-Apiose, L-Rhamnose, L-arabinose and Rutinose, in considerations, whereby D glucose is particularly preferred.

Als Glykoside (Z-O-Rm) kommen als Zuckerbestandteil Monosaccharide (wie die im vorhergehenden Absatz genannten) enthaltende Verbindungen, insbesondere Arbutin, < RTI ID=6.1> Fragilin</RTI> und Poplin, aber auch Oligo-oder Polysaccharide enthaltende Glykoside wie Alkylpoly glucoside, particular APG (handle < RTI ID=6.2> KGaA), < /RTI> in considerations.

Geeignet im Sinne der Erfindung sind Verbindungen, bei denen der Glykosid-Anteil (Z < RTI ID=6.3> O-Rm)</RTI> Arbutin (D. h. m = 1), AC the acyl radical cis, trans, 9,11-oder cis, cis, 9,11 Octadecadiensäure und n 1 are. Gleichfalls geeignet sind solche Verbindungen, bei denen der < RTI ID=6.4> Glykosid-Anteil (Z-O-Rm) Fragilin</RTI> (d. h. m = 1), AC the acyl radical cis, trans, 9,11-oder cis, cis, 9,11-Octadecadiensäure and n of the 1 is.

Other favourable bonds are esters, whereby the Glykosid portion < RTI ID=6.5> (Z-O-Rm) < /RTI> Arbutin (D. h. m = 1), Ac der Acylrest der cis, trans, 9,11-oder der cis, cis, 9,11 Octadecadiensäure und n 2 ist ; Ester, whereby < RTI ID=6.6> Glykosid portion (Z-O-Rm) Fragilin< /RTI> (d. h. m = 1), AC the acyl radical cis, =trans, 9,11-oder cis, cis, 9,11-Octadecadiensäure and n of the 2 is; Verbindungen, bei denen der Glykosid-Anteil < RTI ID=6.7>(Z-O-Rm)</RTI> Arbutin or Fragilin (D. h. m = 1), AC the acyl radical of the Stearidonsäure and n 1 is; schliesslich Verbindungen, wobei der Glykosid-Anteil < RTI ID=6.8>(Z-O-Rm)</RTI> Arbutin or Fragilin (D. h. m = 1), Ac der Acylrest der Stearidonsäure und n 2 ist.

Other favourable bonds are esters with the subsequent parameters: if n = 1 is, the single remainder of AC to a primary OH-group of the sugar bound, in particular to that primary OH-group, which sits at the sugar moiety, is bound to which also R, if m < RTI ID=6.9> w< /RTI> 0 ; if n = 2 is, a remainder of AC to that primary OH-group, which sits at the sugar moiety, is bound to which also R, if m < RTI ID=6.10> X< /RTI> 0, and the other remainder of AC is to a further primary or to a secondary OH-group of the sugar bound.

Particularly preferred bonds according to the present invention are the subsequent esters 1 to 30, with which both m and n are 1, with those AC, Z and R the subsequent importances have and with those the ester group over the primary alcohol group of the sugar/Glykosids formed become (are several Glucose-bzw.

Zucker-Einheiten vorhanden, liegt die Veresterung am primären OH der Glucose Einheit vor, die auch glykosidisch verknüpft ist mit z. B. < RTI ID=7.1>CH3-(CH2) 10-CH2OH)</RTI> :

1. AC is cis, trans, 9,11-Octadecadienoyl; Z is D glucose; is H; 2. AC is cis, cis, 9,11-Octadecadienoyl; Z is D glucose; R is H;
3. AC is trans, cis, 10,12-Octadecadienoyl; Z is D glucose; R is H; 4. AC is cis, trans, 9,11-Octadecadienoyl; Z is D glucose; R ist-para-C6H4-OH;
5. AC is cis, cis, 9,11-Octadecadienoyl; Z is D glucose; R ist-para-C6H4-OH; 6. AC is trans, cis, 10,12-Octadecadienoyl; Z is D glucose; R < RTI ID=7.2> ist-para-C6H4-OH< /RTI> ; 7. Ac ist cis, trans, 9,11-Octadecadienoyl ; Z is D glucose; R is < (CH2); RTI ID=7.3> rxCH3< /RTI> ;
8. AC is cis, cis, 9,11-Octadecadienoyl; Z ist D-Glucose ; R ist (CH2) < RTI ID=7.4>11CH3</RTI> ;
9. Ac ist trans, cis, 10,12-Octadecadienoyl ; Z is D glucose; R ist < RTI ID=7.5>(CH2)</RTI> < RTI ID=7.6> 11CH3< /RTI> ;
10. AC is cis, trans, 9,11-Octadecadienoyl; Z ist (D-Glucose) 2 ; R ist (CH2) < RTI ID=7.7>1rCH3</RTI> ; < RTI ID=7.8> 11.< /RTI> AC is cis, cis, 9,11-Octadecadienoyl; Z is < (D glucose); RTI ID=7.9> 2< /RTI> ; R is < (CH2); RTI ID=7.10> arCH3< /RTI> ;
12. AC is trans, cis, 10,12-Octadecadienoyl; Z is (D glucose) 2; R is < RTI ID=7.11> (CH2) r1CH3< /RTI> ;
13. Ac ist cis, trans, 9,11-Octadecadienoyl ; Z is (D glucose) 3; R ist (CH2) < RTI ID=7.12>11CH3</RTI> ;
14. AC is cis, cis, 9,11-Octadecadienoyl; Z is (D glucose) 3; R ist (CH2) < RTI ID=7.13>11CH3</RTI> ;
15. AC is trans, cis, 10,12-Octadecadienoyl; Z is (D glucose) 3; R is < (CH2); RTI ID=7.14> 11CH3< /RTI> ;
16. Ac ist cis, trans, 9,11-Octadecadienoyl ; Z is (D glucose) 4; R is < (CH2); RTI ID=7.15> 11CH3< /RTI> ;
17. AC is cis, cis, 9,11-Octadecadienoyl; Z is (D glucose) 4; R is < (CH2); RTI ID=7.16> 11CH3< /RTI> ;
18. AC is trans, cis, 10,12-Octadecadienoyl; Z is (D glucose) 4; R is < (CH2); RTI ID=7.17> 11CH3< /RTI> ;
19. AC is cis, trans, 9,11-Octadecadienoyl; Z is (D glucose) 5; R is < (CH2); RTI ID=7.18> 11CH3< /RTI> ; 20. AC is cis, cis, 9,11-Octadecadienoyl; Z is (D glucose) 5; R is < (CH2); RTI ID=7.19> 11CH3< /RTI> ; 21. AC is trans, cis, 10,12-Octadecadienoyl; Z is (D glucose) 5; R is < RTI ID=7.20> (CH2) < /RTI> < RTI ID=7.21> 11CH3< /RTI> ; 22. AC is cis, trans, 9,11-Octadecadienoyl; Z is (D glucose) 6; R is < (CH2); RTI ID=7.22> 11CH3< /RTI> ; 23. AC is cis, cis, 9,11-Octadecadienoyl; Z is (D glucose) 6; R ist (CH2) < RTI ID=7.23> 11CH3< /RTI> ; 24. AC is trans, cis, 10,12-Octadecadienoyl; Z is (D glucose) 6; R is < (CH2); RTI ID=7.24> 11CH3< /RTI> ; 25. AC is cis, trans, 9,11-Octadecadienoyl; Z is < RTI ID=7.25> (D glucose) 7< /RTI> ; R is < RTI ID=7.26> (CH2) nCH3< /RTI> ; 26. Ac ist cis, cis, 9,11-Octadecadienoyl ; Z is (D glucose) 7; R is < (CH2); RTI ID=7.27> 11CH3< /RTI> ; 27. AC is trans, cis, 10,12-Octadecadienoyl; Z is (D glucose) 7; R is < RTI ID=7.28> (CH2) < /RTI> < RTI ID=7.29> 11CH3< /RTI> ; 28. AC is 6,9,12,15-Octadecatetraenoyl (6Z, 9Z, 12Z, 15Z); Z is D glucose; R is H; 29. AC is 6,9,12,15-Octadecatetraenoyl (6Z, 9Z, 12Z, 15Z); Z is D glucose; R be p < RTI ID=7.30> C6H4-OH< /RTI> ; 30. AC is 6,9,12,15-Octadecatetraenoyl (6Z, 9Z, 12Z, 15Z); Z is D glucose; and R is < RTI ID=8.1> (CH2) 11 CH3- < /RTI>

Further preferred bonds are the esters 31 to 60, itself from the esters the 1 to < RTI ID=8.2> 30< /RTI> lediglich dadurch unterscheiden, dass die Zuckereinheit (en) nicht aus D-Glucose, sondern aus der entsprechenden Anzahl von D-Galactose-Einheiten besteht. The ester

54 is thus, in order to give an example, an analogue to the esters 24 and thus an ester, with the AC of trans, cis, 10,12-Octadecadienoyl; Z (D-Galactose) 6; R < RTI ID=8.3> (CH2) ?CH3< /RTI> ; m and n 1 are.

Preferred ones are also the subsequent esters 61 to 120 in analogy to the esters 1 to 60, which differ however from the latters by the fact that n = 2 and that the second AC remainder at the 4-OH Glucose-bzw. Galactose-Einheit sitzt.

Weiterhin bevorzugt sind die folgenden Ester 121 bis 180 in Analogie zu den Estern 61 bis 120, die sich allerdings von letzteren dadurch unterscheiden, dass der zweite Ac Rest nicht am 4-OH, sondern am 1-OH der Glucose-bzw. Galactose unit sits.

Likewise preferred is the subsequent esters 181 to 240 in analogy to the esters 121 to 180, which differ however from the latters by the fact that the second AC remainder not at the 1-OH, but at the 2-OH Glucose-bzw. Galactose unit sits.

Weitere bevorzugte Ester sind die folgenden Ester 241 bis 300 in Analogie zu den Estern 1 bis 60, die sich allerdings von letzteren dadurch unterscheiden, dass n = 3 und dass diese < RTI ID=8.4> Verknüp-fungen</RTI> at the primary (6-OH) as well as the 1-OH-und of the 4-OH group of the sugar take place.

Other preferred esters are the subsequent esters 301 to 360 in analogy to the esters 241 to 300, which differ however from the latters by the fact that the three AC remainders at the primary as well as the 2-OH-und of the 4-OH-Gruppe of the sugar are bound.

Wiederum andere bevorzugte Ester sind die folgenden Ester 361 bis 420 in Analogie zu den Estern 1 bis 60, die sich allerdings von letzteren dadurch unterscheiden, dass n = 4 und dass diese Verknüpfungen an der primären (6-OH-) sowie der 1-OH-, der 2-OH und der 4-OH-Gruppe des Zuckers erfolgen.

By the inventive modification of the fatty acids, D. h. by the described above derivatization of the fatty acids in form of the junctions of the present invention, the compatibility as well as the biological availability and effect of such fatty acids for the inset in Kosmetik, pharmacy and/or diet are improved.

Dementsprechend betreffen weitere Aspekte der vorliegenden Erfindung die Verwendung der Verbindungen der allgemeinen Formel < RTI ID=9.1> (I) < /RTI> zur Herstellung von kosmetischen und pharmazeutischen Zubereitungen, ihre Verwendung als Additive zu Nahrungs-, < RTI ID=9.2> Nahrungsergänzungs- und < /RTI> Feeds. Weitere Aspekte der vorliegenden Erfindung betreffen pharmazeutische und kosmetische Zubereitungen sowie Nahrungs-, < RTI ID=9.3> Nahrungsergänzungs- und < /RTI> Feed, which < at least a connection of the general formula; RTI ID=9.4> (I) < /RTI> contained.

A further subject matter of the invention is therefore a method < to the production of the inventive bonds of the formula; RTI ID=9.5> (I), < /RTI> by the fact the characterized is that a sugar Z and/or a Glykosid < RTI ID=9.6> Z-O-Rm < /RTI> mit einer ungesättigten Fettsäure < RTI ID=9.7> AcOH < /RTI> oder mit einem Ester, vorzugsweise einem Methyl- oder Ethylester, dieser Fettsäuren AcOH in Gegenwart einer Lipase verestert wird.

Among the suitable enzymatic catalysts to the esterification (by means of transesterification) the hydrolase, the particular Lipasen rank of the acids and alcohol components mentioned like the Lipasen from *Candida antarctica*, *Candida rugosa* (formerly *Candida cylindracea*), *Geotrichum candidum*, *Aspergillus niger*, *Penicillium roqueforti*, *Rhizopus* < RTI ID=9.8> *arrhizus* < /RTI> and *Mucor miehei*.

A preferred Lipase is the Lipase (ISO enzyme B) from *Candida antarctica*, for which there are two reasons. First of all it particularly shows one high selectivity with the esterification of the acetals with the insatiated fatty acids, although these do not rank among their typical substrates. Des weiteren zeigt sie keine Grenzflächenaktivierung (ein entscheidendes Merkmal zur Klassifizierung von Hydrolasen in die Gruppe der Lipasen), da ihr ein wichtiges < RTI ID=9.9> Lipasestrukturmerkmal, < /RTI> a movable Peptidkette at the active center < RTI ID=9.10> (so-called. lid) fehlt. < /RTI>

Es wird also die selektive Veresterungseigenschaften einiger Enzyme (siehe Beschreibung), insbesondere Lipase aus *Candida* < RTI ID=10.1> *antarctica* Isoenzym B, < /RTI> in addition used, To link and partly improve active substances with one another to esters and so the effects and a simultaneous possibility to have of isolating the most active isomer of the CLAs from the mixture.

Gerade die gezielte Veresterung ist aber für die biologische Verfügbarkeit und Compatibility of the inventive materials crucial. The chemical Synthese führt jedoch aufgrund mangelnder Regioselektivität zu groben Product mixtures. Therefore is the here described enzymatic (see examples) mild and regioselective synthesis of advantage. Inventive one means regiospezifisch that only a certain OH-group of a polyole becomes third.

Corresponding one means regioselektiv that a certain OH-group of a polyole does not become preferred, but exclusive, third.

The inventive connections are < RTI ID=10.2> Formula (I) < /RTI> erst einmal mittels des erfindungsgemäßen Verfahrens hergestellt worden, muss in aller Regel ein Verfahren folgen, < RTI ID=10.3> um = die gewünschte < /RTI> (n) To up-to-some connection (EN). Thus a further subject matter of the present invention consists of it, a method to the purification of the bonds of the formula < RTI ID=10.4> (I) < /RTI> to make available, which is characterized thereby that it concerns an aqueous two-phase extraction procedure with organic solvents, with which the target compound from the not converted fatty acids separated become selective can. Vorzugsweise handelt es sich bei dem organischen Lösungsmittel um n-Hexan, Cyclohexan, THF, Diethylether. Alternative one knows the purification also by a chromatographic method at silicagel, preferably with < RTI ID=10.5> Ethyl acetate/methanol oder < /RTI> Dichloromethane/methanol mixtures with minor proportions acetic acid and/or water takes place, which can become also additional an aqueous two-phase extraction procedure with organic solvents performed.

Since the inventive esters of the formula < RTI ID=10.6> (I) < /RTI> a good biological availability and effect have, can it in cosmetic and pharmaceutical preparing and/or as food additives be used with the result that the quality of these products becomes remarkably improved.

Die erfindungsgemäßen Ester der konjugierten Linolsäuren (CLAs) weisen eine < RTI ID=11.1> antiinflammatorische, < /RTI> antipyretische, antiphlogistische und/oder analgetische Wirkung auf und haben über-dies auch antioxidative, < RTI ID=11.2> hautaufhellende < /RTI> or antibacterial/antiviral effects. Die < RTI ID=11.3> Fettdepot-reduzierende < /RTI> Effect of the CLAs shows up likewise in the inventive connections.

Since the connections of the formula < RTI ID=11.4> (I) < /RTI> a good biological availability and effect have, can it in cosmetic and pharmaceutical preparing and/or as food additives be used with the result that the quality of these products becomes remarkably improved.

Beyond that the inventive connections are particularly good into lipophilic Basis prescriptions trainable and can be formulated in a simple manner as stable emulsions.

Accordingly the inventive connections of the formula are < RTI ID=11.5> (I) < /RTI> to the production of cosmetic and/or pharmaceutical preparing and/or Nahrungs- bzw. Feeds uses.

Further subject matters of the invention are < thereafter the use of the connections; RTI ID=11.6> Formula (I) < /RTI> zur Herstellung von kosmetischen und/oder pharmazeutischen Zubereitungen ; the use as food auxiliary or additives in food preparing and in feeds (z. B. für die Tierzucht) ; cosmetic and pharmaceutical preparing as well as food preparing and feed, which (one) < connection (EN) of the formula; RTI ID=11.7> (I) < /RTI> contained.

Die unter erfundungsgemässer Verwendung der Verbindungen < RTI ID=11.8> (I) </RTI> available cosmetic preparing such as hair shampoos, < RTI ID=11.9> Hair lotions, < /RTI> Foam baths, < RTI ID=11.10> Showers, < /RTI> Creams, gels, lotions, alcoholic and < RTI ID=11.11> aqueous/alcoholic solutions, < /RTI> Emulsionen, < RTI ID=11.12> Wachs/Fett-Massen, </RTI> Furthermore pin preparations, powders or ointments, know as further Hilfs-und of additives mild surfactants, < RTI ID=11.13> Okörper, < /RTI> Emulsifying agents, < RTI ID=11.14> Over greasing means, < /RTI> Periglanzwachse, consistency giver, < RTI ID=11.15> Thickener, < /RTI> Polymers, silicone compounds, fats, wax, stabilisers, biogenous active substances, Deo active substances, anti shed means, film former, swelling agent, UV light protection factors, Antioxidantien, Hydrotrope, < RTI ID=12.1> Preservative, Insektenrepellentien, selfbrown, Solubilisatoren, < /RTI> Perfume oils, dyes, germ-inhibitive means and such contained.

The quantity required of the inventive connections in the cosmetic preparing lies usually within the range of 0,01 to 5 Gew. - %, preferably however from 0,1 to 1 Gew. - % related to the total quantity of the preparing.

To the production of pharmaceutical or also cosmetic preparing the inventive bonds of the general formula (1) leave themselves, if necessary in combination with other active substances, together with to one or more inert usual carrier materials and/or diluents, z. B. with corn strength, lactose, cane sugar, micro-crystalline cellulose, magnesium stearate, < RTI ID=12.2> Polyvinylpyrrolidone, citric acid, tartaric acid, < /RTI> Water, < RTI ID=12.3> Water/ethanol, < /RTI> < RTI ID=12.4> Water/Glycerin, < /RTI> Waters/sorbitol, water/polyethylene glycol, propylene glycol, carboxymethylcellulose or fetthaltigen materials such as hard fat or their suitable mixtures, into usual galenische preparing such as tablets, dragees, nacelles, powders, suspensions, drops, ampoules, juices or suppositories train.

The daily dosage required for the achievement of a corresponding effect with pharmaceutical applications appropriately 0.1 to 10 amounts to mg/kg body weight, preferably 0.5 to 2 mg/kg body weight.

The food spare and additives as, available under inventive use of the connections of the formula (I), < RTI ID=12.5> Sportier Drinks < /RTI> contained suitable-proves the connection (EN) < RTI ID=12.6> Formula (I) < /RTI> in a quantity, which leads with a usual need at Flüssigkeitsaufnahme from 1 to 5 litres per day to a dosage of these bonds from at 0.1 to 10 mg, preferably 0.5 to 5 mg, per kg body weight. An exemplary use in food industry exists for the connections of the formula < RTI ID=12.7> (I) < /RTI> < RTI ID=12.8> as Färbe-und/or Gewürzstoffe. < /RTI>

Examples example 1: CLA + glucose < RTI ID=13.1> 6-O-cis9, < /RTI> trans-11-Octadecadienoyl-D-glucopyranose 19,8 g (0,1 mol) < RTI ID=13.2> D (+) - glucose, < /RTI> 39,6 g CLA (60% conjugated Linolsäure) (Edenor UKD 6010), 30 < RTI ID=13.3> g < /RTI> Molecular sieve, 120 ml t-Butanol and 3g immobilized Lipase B out Candida antartica were < 48 hours with 60 C with 400 RPM at the magnet agitator in 300; RTI ID=13.4> ml Erlenmeyerkolben < /RTI> inkubiert. The conversion became by means of Thin layer chromatography (silicagel 60-Platten with < RTI ID=13.5> Fluoreszenzindikator < /RTI> ; Laufmittel: < RTI ID=13.6> Ethyl acetate/Methanol < /RTI> 10 : 1, v/v and Dichlormethan/Methanol/Essigsäure 95: 5 : 0.1, v/v/v; Visualization: UV detection as well as by means of acetic acid < RTI ID=13.7> Sulphuric acid/anisic aldehyde Tauchreagenz < /RTI> (100 : 2 : 1, < RTI ID=13.8> v/v/v) < /RTI> proven. The product became with 300 ml THF extracted and over column chromatography (silicagel F60; Laufmittel: Ethyl acetate/methanol 10: 1, v/v) purified. After cleaning the yield amounted to 43 g (37,3%) (very viscous product). The ratio from cis trans isomer to cis cis isomer amounts to 1: 0.4.

Rf-value: 0.41 < RTI ID=13.9> (Ethyl acetate/Methanol < /RTI> 10 : 1) 0.05 (dichlormethane/methanol/acetic acid 95: 5 : 0.1) < RTI ID=13.10> 13C-NMR < /RTI> (100,6 MHz, CD30D): < RTI ID=13.11> 8< /RTI> = (cis trans isomer) 14,4 < RTI ID=13.12> (C-18), < /RTI> 23,8 < RTI ID=13.13> (C-17), < /RTI> 25,8 (C3) 28,0 (C-8), 30,1-30,7 < RTI ID=13.14> (C-4, < /RTI> C-5, C-6, C-7, < RTI ID=13.15> C-14, C-15, C-16), < /RTI> 32,8 < RTI ID=13.16> (C-13), < /RTI> 34,6 (C-2), 64,8 < RTI ID=13.17> (C-6'), < /RTI> 70,4 (C-4'), 71,8 < RTI ID=13.18> (C-5'), < /RTI> 73,8 < RTI ID=13.19> (C-2'), < /RTI> 74,9 < RTI ID=13.20> (C-3'), < /RTI> 93,8 (C-1'), 129,7 < RTI ID=13.21> (C-10), < /RTI> 130,2 < RTI ID=13.22> (C-11), < /RTI> 130,5 < RTI ID=13.23> (C-12), < /RTI> 131,6 (C-9), 173,6 (c1).

< RTI ID=13.24> 8< /RTI> = (cis cis isomer) 14,4 (C-18), 23,8 (C-17), 25,6 (C-3) 30,1-30,7 (C-4, C-5, C-6, C-7, < RTI ID=13.25> C-14, C-15, C-16), < /RTI> 32,6 < RTI ID=13.26> (C-13), < /RTI> 33,6 (C-8), 34,4 (C-2), 64,8 < RTI ID=13.27> (C-6'), < /RTI> 70,4 < RTI ID=13.28> (C-4'), < /RTI> 71,8 (C< RTI ID=13.29> 5'), < /RTI> 73,8 < RTI ID=13.30> (C-2'), < /RTI> 74,9 < RTI ID=13.31> (C-3'), < /RTI> 93,8 < RTI ID=13.32> (C-1'), < /RTI> 126,8 (C-11) 129,7 (C-10), 130,2 (C-9), 131,6 (C-12), 174,8 (c1).

< RTI ID=13.33> Beispiels 2: < /RTI> CLA + Alkylpolyglykosid (APG) < RTI ID=13.34> 6-O-cis-9, trans-11-Octadecadienoyl-alkylglucosid < /RTI> 2g APG (handle < RTI ID=13.35> KGaA), < /RTI> 15g Edenor UKD6010, 4,5 g Molekularsieb, 10 < RTI ID=13.36> ml t-Butanol < /RTI> and 4,5 g immobilized Lipase B from Candida antartica were inkubiert 48 hours with 60 C with 100 RPM at the magnet agitator in 250 ml Erlenmeyer flasks. The conversion was < by means of; RTI ID=13.37> thinschichtchromatographie < /RTI> (Silicagel 60-Platten with < RTI ID=13.38> Fluoreszenzindikator < /RTI> ; Laufmittel: Ethyl acetate 100%, visualization: UV-Detektion sowie mittels < RTI ID=14.1> Essigsäure/Schwefelsäure/Anisaldehyd-Tauchreagenz < /RTI> (100 : 2 : 1 v/v/v)). The product over an aqueous two-phase extraction in the hexane phase enriched, one in-rotated and over column chromatography (silicagel F60; Laufmittel < RTI ID=14.2> Ethyl acetate/Methanol < /RTI> (10 : 1, v/v)) gereinigt. EMI 14.1

Rf-value: 0.74 < RTI ID=14.3> (Ethyl acetate/Methanol < /RTI> 10 : 1) < RTI ID=14.4> Example 3: Stearidonsäureethylester < /RTI> + Arbutin Arbutin EMI 14.2

6,9,12,15-Octadecatetraenoyl (6Z, 9Z, < RTI ID=14.5> 12Z, 15Z) - Arbutin < /RTI> 1,36 g (5 mmol) Arbutin, < RTI ID=14.6> 40g Stearidonsäureethylester, < /RTI> 4,5 g molecular sieve, 10 ml t-Butanol and 4,5 g immobilized Lipase B from Candida antartica were < 48 hours with 60; RTI ID=14.7> C< /RTI> with 100 RPM at the magnet agitator in 300 ml Erlenmeyer flasks inkubiert. The conversion became by means of thin layer chromatography (silicagel < RTI ID=14.8> 60-Platten < /RTI> with fluorescence indicator; Laufmittel: Ethylacetat 100 %, < RTI

ID= 14.9> Visualisierung</RTI> : UV detection as well as by means of acetic acid/sulphuric acid/anisic aldehyde dipping reagent (100: 2 : 1, < RTI ID=14.10> v/v/v))< /RTI> proven. The product became over Säulenchromatographie (silicagel F60; Laufmittel: Ethylacetat/2-Propanol 10: 1, v/v) purified.

< RTI ID= 14.11> Ru-vert</RTI> : 0.35 (ethyl acetate 100%)



Claims of WO0179241

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Claims

1. Connections of the general formula (1): < RTI ID=15.1> Acr, - O-Z-0-R, < /RTI> (1), where R a hydrogen, a one over one; RTI ID=15.2> Etherbrücke< /RTI> at the sugar bound branched or straight-chain < RTI ID=15.3> C8-C20-Alkyl, < /RTI> one Arylalkyl or a substituted or a unsubstituierten < RTI ID=15.4> C6-C, o-aryl radical represents, < /RTI> where Z (sugar) stands for a mono, a disaccharide or a polysaccharide, which are n-multiple ester-like with AC substituted and, if R does not stand for hydrogen, acetalisch to the remainder R bound, where AC a multiple insatiated < RTI ID=15.5> C 5-C25-Acylrest< /RTI> with at least 4 insulated and/or at least two conjugated double bonds or it represents an aryl-aliphatic remainder with 1-4 groups of groupgroups between group of esters and aromatic ring where m an integral number (1.2.3,?) including 0 it is where n an integral number (1.2.3,?), however 0, is not <, with that; RTI ID=15.6> Condition that Z-O-Rm< /RTI> not for Salicin, that is 2-Hydroxymethyl-phenyl) - glucopyranosid, stands.
2. The bonds of claim 1, whereby Z a monosaccharide, in particular D Glucose, D-Galactose, D-xylose, D-Apiose, L-Rhamnose, L-arabinose and Rutinose, are.
3. The connections of claim 1 or 2, whereby < RTI ID=15.7> Glykosid portion (Z-O-Rm) < /RTI> such is, that as a sugar component a monosaccharide, in particular in Monosaccharide according to claim 2, contained bonds, in particular Arbutin, < RTI ID=15.8> Fragilin< /RTI> and Poplin.
4. The connections of claim 1 or 2, whereby the Glykosid portion < RTI ID=15.9> (Z-O-Rm) < /RTI> such is, that as a sugar component Oligo or a polysaccharide how Alkylpolyglucoside, particular APG < RTI ID=15.10> (Handle KGaA), < /RTI> is.
5. The bonds of one of the preceding claims, whereby the linkage of AC at the sugar over a primary alcohol group of the sugar made.
6. The connections of one of the preceding claims, whereby that Glykosid Portion < RTI ID=16.1> (Z-O-Rm) < /RTI> Arbutin, Populin or < RTI ID=16.2> Fragilin< /RTI> is.
7. The connections of one of the preceding claims, whereby AC is the acyl radical of one of the subsequent fatty acids: a CLA or a Stearidonsäure, in particular those Octadecadiensäuren, those over conjugated double bonds at the C-atoms 9 and 11,10 and 12 or 11 and 13 orders, in particular cis, trans, 9,11-und cis, cis, 9,11-Octadecadiensäure.
8. The connections of one of the preceding claims, whereby that Glykosid Portion < RTI ID=16.3> (Z-O-Rm) < /RTI> Arbutin (D. h. m = 1), whereby AC the acyl radical cis, trans, 9,11-oder cis, cis, 9,11-Octadecadiensäure and whereby n 1 is.
9. The connections of one of the claims 1 to 7, whereby the Glykosid portion < RTI ID=16.4> (Z-O-< /RTI> Rm) Fragulin (D. h. m = 1), whereby AC the acyl radical cis, trans, 9,11-oder cis, cis, 9,11-Octadecadiensäure and whereby n 1 is.

& top < RTI ID=16.5> 10.< /RTI> The connections of one of the claims 1 to 7, whereby < RTI ID=16.6> Glykosid portion (Z-O-< /RTI> Rm) Arbutin (D. < RTI ID=16.7> h.< /RTI> m = 1), whereby AC the acyl radical cis, trans, 9,11-oder cis, cis, 9,11-Octadecadiensäure and whereby n 2 is.

< RTI ID=16.8> 11.< /RTI> The connections of one of the claims 1 to 7, whereby the Glykosid portion < RTI ID=16.9> (Z-O-< /RTI> Rm) Fragulin (D. h. m = 1), whereby AC the acyl radical cis, trans, 9,11-oder cis, cis, 9,11-Octadecadiensäure and whereby n 2 is.

12. The connections of one of the claims 1 to 7, whereby < RTI ID=16.10> Glykosid portion (Z-O-< /RTI> Rm) Arbutin or Fragilin (D. h. m = 1), whereby AC the acyl radical of the Stearidonsäure and whereby n 1 is.

< RTI ID=17.1> 13.< /RTI> The connections of one of the claims 1 to 7, whereby the Glykosid portion (Z-O-Rm) Arbutin or < RTI ID=17.2> Fragulin< /RTI> (D. h. m = 1), whereby AC the acyl radical of the Stearidonsäure and whereby n 2 is.

14. Connections of one preceding claims, whereby, if n = 1, which is single remainder of AC to a primary OH-group of the sugar bound, in particular to that primary OH-group, which sits at the sugar moiety, to which also R bound it is, if m < RTI ID=17.3> w< /RTI> 0, and whereby, if n = 2, a remainder of AC to that primary OH-group, which sits at the sugar moiety, to which also R bound is, if m < RTI ID=17.4> #< /RTI> 0, and which is other remainder of AC to a further primary or to a secondary OH-group of the sugar bound.

< RTI ID=17.5> 15.< /RTI> Method to the production of the bonds < RTI ID=17.6> Formula (I) < /RTI> of one of the preceding claims, characterised in that a sugar Z and/or.
Glykosid < RTI ID=17.7> Z-O-Rm< /RTI> with an insatiated fatty acid < RTI ID=17.8> AcOH< /RTI> or with an ester, preferably one methyl or ethyl ester, these fatty acids < RTI ID=17.9> AcOH< /RTI> in presence of a hydrolase third or one umgeestert.

16. The method of claim 15, whereby the hydrolase a Lipase, in particular a Lipase from *Candida rugosa* (formerly *Candida cylindracea*), *Candida antarctica*, *Geotrichum candidum*, *Aspergillus niger*, *Penicillium roqueforti*, *Rhizopus arrhizus* and *Mucor miehei*, in particular the Lipase < RTI ID=17.10> (Isoenzym< /RTI> B) from *Candida antarctica*, is.

17. The method of claim 15 or 16, whereby itself to the esterification reaction
Step to the purification of the bonds of the formula (I) attaches, either the aqueous two-phase extraction procedure with organic solvents such as n-hexane, cyclohexane, THF or < RTI ID=17.11> Diethylether< /RTI> or a chromatographic Method at silicagel, preferably with < RTI ID=17.12> Ethyl acetate/methanol oder< /RTI> Dichloromethane/methanol mixtures with minor proportions acetic acid and/or Water, is.

18. Cosmetic or pharmaceutical composition or Nahrungs-bzw.

Nahrungsergänzungs or feed composition, contained at least one of the connections of one of the claims 1 to 14.